REMARKS

Claims 1-26 are pending in the application. Claims 2-14, 16-23 and 25 are newly amended to comply with US patent practice. The amendments are not believed to add new matter. Support for the amendments is found within each claim.

Claims 1-9 were previously amended on July 12, 2001 during international examination. Claims 3-15, 18-21 and 23-26 were later amended in a preliminary amendment filed January 29, 2002. A copy of:

1) the PTO date-stamped return postcard dated January 29, 2002 showing receipt of the preliminary amendment,

2) a copy of the as-filed preliminary amendment; and,

3) a copy of the substitute sheet containing amended claims 1-9, filed July 12, 2001 and submitted to the US PTO as part of the National Phase filing are attached for the convenience of the Examiner. It would appear from the Office Action text that the Examiner has not based the restriction requirement on the claims as previously amended.

The Examiner should note that amended claim 15 now depends from claim 1:

"Claim 15. A method of detecting a nucleic acid sequence of interest in a sample, the method comprising the steps of: contacting a nucleic acid probe molecule in accordance with [~~any one of the preceding claims~~] claim 1 with a nucleic acid target molecule...". Other claims were amended as indicated in the current listing of the claims.

Restriction Requirement

Reconsideration and withdrawal of the requirement is respectfully requested. The Office Action restricted pending claims 1-26 into the following groups:

1. Group I, claims 1-14, 24 and 25, drawn to a single stranded nucleic acid probe.
2. Group II, claims 15-23 and 26, drawn to a method of detecting a nucleic acid sequence.

Applicants respectfully traverse the restriction requirement. The Office asserts the inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because the groups allegedly lack the same or corresponding special technical feature. The Office asserts the claimed invention fails to make a contribution over the prior art because Clueziat *et al.* (USPN 5,874,260, filed 02/23/99) [Clueziat] allegedly "teaches the kind of probe as claimed (Office, citing to Figure 1, column 11 and column 13 of Clueziat) in claim 1." According to the Office, a special technical feature is allegedly lacking between Groups I and II since the methods of claim 15 are not limited so as require the probe of claim 1.

However, the Office has not explicitly pointed out where, for example, Clueziat teaches or suggests a probe molecule having, *inter alia*, "..a blocking moiety, there being from 0 to 50 nucleic acid bases between the blocking moiety and the promoter sequence" as is claimed in amended claim 1. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute." The Office has not provided reasons for anticipation as well as a motivational statement regarding obviousness. Thus, claim 1, and claims dependent therefrom, do in fact have a special technical feature which make a contribution over the prior art.

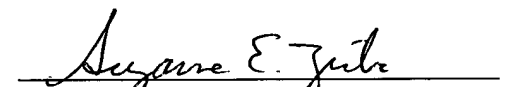
In addition, claim 15 was previously amended by the January 29, 2002 amendment to depend from claim 1. Thus, the Office arguments regarding the lack of limitation of claim 15 so as to require the probe of claim 1 are moot. Since Group II claims are linked to Group I by the special technical feature of Group I, Group II should be examined along with the entirety of Group I.

It is respectfully requested that the claims set forth in Group II be joined to, and examined with, the claims of elected Group I. Reconsideration and withdrawal of the requirement for restriction is respectfully requested.

It is believed the application is in condition for examination on the merits and such is respectfully requested. If, in the opinion of the Examiner, an interview would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the telephone number provided below.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. § 1.16 and § 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **Constructive Petition for Extension of Time** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,
Morgan, Lewis & Bockius LLP



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PLEASE STAMP AND RETURN TO SHOW RECEIPT OF:
National Stage of International Application No. PCT/GB00/02946 under 35 U.S.C. 371

For: METHOD FOR AMPLIFICATION OF NUCLEIC ACIDS

Inventors: **John Scott LLOYD et al.**

BOX PCT

1. **Please charge Deposit Acct. No. 50-0310 in the amount of $499.00**
2. Transmittal Letter concerning a filing under 35 U.S.C. § 371.
3. WO 01/019376 with a total of 41 pages, including 4 pages of claims and 8 pages of Sequence Listing and 13 sheets of drawings
4. Preliminary Amendment
5. PCT/IPEA/409
6. PCT/IB/304
7. PCT/IB/308
8. Information Disclosure Statement
9. International Search Report
10. PTO-1449, 5 documents as listed
11. Statement Accompanying Sequence Listing
12. Diskette containing Sequence Listing CRF
13. Paper Copy of Sequence Listing

Dated: January 29, 2002
Attorney Docket No.: 056222-5008
ECW/lmp

3

Claims

1. A probe molecule comprising single stranded nucleic acid; said probe comprising a single stranded sequence complementary to a target nucleic acid sequence; a single strand of an RNA polymerase promoter sequence, and a blocking moiety, there being from 0 to 50 nucleic acid bases between the blocking moiety and the promoter sequence.

2. A probe according to claim 1, comprising the template strand of an RNA polymerase promoter.

3. A probe according to claim 1 or 2, comprising a –5 sequence adjacent to the 3' end of the promoter sequence.

4. A probe according to any one of claims 1, 2 or 3, comprising a +12 sequence adjacent to the 5' end of the promoter.

5. A probe according to any one of the preceding claims, such that when hybridised to the target, the 3' end of the target is extendible by a DNA polymerase.

6. A probe according to any one of the preceding claims, wherein the target complementary portion is located 3' of the promoter sequence.

7. A probe according to any one of the preceding claims, wherein a blocking moiety is located between position –19 and –68.

8. A probe according to any one of the preceding claims, wherein a blocking moiety is located between position –19 and –38.

9. A probe according to any one of the preceding claims, wherein a blocking moiety is located between position –22 and –35.

PATENT
Attorney Docket No. 056222-5008

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : John Scott **LLOYD**, et al.	Group Art Unit: Unassigned
U.S. National Phase Application Filed: January 29, 2001	Examiner: Unassigned
U.S. Application No.: To Be Assigned	
Date of National Stage Entry : Concurrently	
Based on PCT/GB00/02946 Filed : July 31, 2000	
For: METHOD FOR AMPLIFICATION OF NUCLEIC ACIDS	

Commissioner for Patents
Washington, D.C. 20231

Sir:

PRELIMINARY AMENDMENT

Prior to the examination of the above-identified application on the merits, please amend the application as follows:

IN THE CLAIMS:

Please substitute the following amended versions of claims 3-15, 18-21 and 23-26 for the original claims.

3. (AMENDED) A probe according to claim 1, comprising a –5 sequence adjacent to the 3' end of the promoter sequence.

4. (AMENDED) A probe according to claim 1, comprising a +12 sequence adjacent to the 5' end of the promoter.

5. (AMENDED) A probe according to claim 1, such that when hybridised to the target, the 3' end of the target is extendible by a DNA polymerase.

6. (AMENDED) A probe according to claim 1, wherein the target complementary portion is located 3' of the promoter sequence.

7. (AMENDED) A probe according to claim 1, wherein a blocking moiety is located between position –19 and - 68.

8. (AMENDED) A probe according to claim 1, wherein a blocking moiety is located between position –19 and –38.

9. (AMENDED) A probe according to claim 1, wherein a blocking moiety is located between position –22 and –35.

10. (AMENDED) A probe according to claim 1, wherein the blocking moiety comprises a C_2-C_{20} alkyl, alkanol or alkylene residue.

11. (AMENDED) A probe according to claim 1, wherein the probe comprises a C_3-C_{10} alkyl, alkanol or alkylene residue.

12. (AMENDED) A probe according to claim 1, comprising an octanediol, propanediol or hexaethylene glycol residue.

13. (AMENDED) A probe according to claim 1, comprising PNA and/or LNA.

14. (AMENDED) A probe according to claim 1, wherein a target complementary

protein of the probe comprises PNA and/or LNA.

15. (AMENDED) A method of detecting a nucleic acid sequence of interest in a sample, the method comprising the steps of: contacting a nucleic acid probe molecule in accordance with claim 1 with a nucleic acid target molecule, which target is the sequence of interest or is formed as a result of the presence in the sample of the sequence of interest; causing extension of the 3' end of the target using the probe as a template, thereby creating a functional double stranded RNA polymerase promoter; causing RNA synthesis from the RNA polymerase promoter, to create an RNA molecule; and detecting directly or indirectly the RNA molecule so produced.

18. (AMENDED) A method according to claim 16, wherein the sequence of the further RNA molecule is substantially similar to that of the original target molecule, such that the further RNA molecule is able to hybridise, under the assay conditions employed, to the original nucleic acid probe molecule.

19. (AMENDED) A method according to claim 16, wherein the target sequence comprises DNA or RNA.

20. (AMENDED) A method according to claim 16, wherein the target sequence is DNA or RNA formed as a result of the presence in the sample of the nucleic acid sequence of interest.

21. (AMENDED) A method according to claim 16, wherein the RNA molecule is detected directly or indirectly by means of a labelled binding partner.

23. (AMENDED) A method according to claim 21, wherein the labelled binding

partner comprises DNA, RNA, LNA, PNA, or any combination thereof.

24. (AMENDED) A kit for use in performing a method of detecting a nucleic acid sequence of interest, comprising a probe molecule in accordance with claim 1, and packaging means.

25. (AMENDED) A kit according to claim 24, further comprising one or more of the following: instructions for performing the method; a buffer; a DNA polymerase; an RNA polymerase; deoxyribonucleotide triphosphates; ribonucleotide triphosphates; and a labelled binding partner.

26. A method of detecting a nucleic acid sequence of interest in a sample, the method comprising the steps of: contacting a nucleic acid probe molecule in accordance with claim 1 with a further probe and with a nucleic acid target molecule, which target is the sequence of interest or is formed as a result of the presence in the sample of the sequence of interest; causing the further probe molecule and the target molecule to hybridise adjacent each other to the probe molecule, thereby creating a functional double stranded RNA polymerase promoter; causing RNA synthesis from the RNA polymerase promoter, to create a RNA molecule; and detecting directly or indirectly the RNA molecule so produced.

REMARKS

Applicants respectfully submit that no prohibited new matter has been introduced by this Preliminary Amendment and that amended claims 1 to 26 are drawn to the same invention as claims 1-26 of International Application PCT/GB00/02946. The changes to the claims represent changes in formalities so as to bring the claims into compliance with the rules of practice in the United States, avoiding improper multiple dependencies and eliminating multiple dependencies so as to reduce costs.

Respectfully Submitted,

MORGAN, LEWIS & BOCKIUS LLP

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Date: January 29, 2002

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MARKED-UP VERSION TO SHOW CHANGES IN CLAIMS

3. **(AMENDED)** A probe according to claim 1 ~~[or 2]~~, comprising a –5 sequence adjacent to the 3' end of the promoter sequence.

4. **(AMENDED)** A probe according to ~~[any one of claims 1, 2 or 3,]~~ **claim 1,** comprising a +12 sequence adjacent to the 5' end of the promoter.

5. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1,** such that when hybridised to the target, the 3' end of the target is extendible by a DNA polymerase.

6. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1,** wherein the target complementary portion is located 3' of the promoter sequence.

7. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1,** wherein a blocking moiety is located between position –19 and - 68.

8. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1,** wherein a blocking moiety is located between position –19 and –38.

9. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1,** wherein a blocking moiety is located between position –22 and –35.

10. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1,** wherein the blocking moiety comprises a C_2-C_{20} alkyl, alkanol or alkylene residue.

11. **(AMENDED)** A probe according to ~~[any one of the preceding claims,]~~

11. **(AMENDED)** A probe according to ~~[any one of the preceding claims,]~~ **claim 1** wherein the probe comprises a C_3-C_{10} alkyl, alkanol or alkylene residue.

12. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1** comprising an octanediol, propanediol or hexaethylene glycol residue.

13. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1**, comprising PNA and/or LNA.

14. **(AMENDED)** A probe according to ~~[any one of the preceding claims]~~ **claim 1**, wherein a target complementary protein of the probe comprises PNA and/or LNA~~[>]~~.

15. **(AMENDED)** A method of detecting a nucleic acid sequence of interest in a sample, the method comprising the steps of: contacting a nucleic acid probe molecule in accordance with ~~[any one of the preceding claims]~~ **claim 1** with a nucleic acid target molecule, which target is the sequence of interest or is formed as a result of the presence in the sample of the sequence of interest; causing extension of the 3' end of the target using the probe as a template, thereby creating a functional double stranded RNA polymerase promoter; causing RNA synthesis from the RNA polymerase promoter, to create an RNA molecule; and detecting directly or indirectly the RNA molecule so produced.

18. **(AMENDED)** A method according to claim 16 ~~[or 17]~~, wherein the sequence of the further RNA molecule is substantially similar to that of the original target molecule, such that the further RNA molecule is able to hybridise, under the assay conditions employed, to the original nucleic acid probe molecule.

19. **(AMENDED)** A method according to ~~[any one of claims]~~ **claim** 16, ~~[17 or 18,]~~ wherein the target sequence comprises DNA or RNA.

20. **(AMENDED)** A method according to ~~[any one of claims 16-19]~~ **claim 16**, wherein the target sequence is DNA or RNA formed as a result of the presence in the sample of the nucleic acid sequence of interest.

21. **(AMENDED)** A method according to ~~[any one of claims 16-20]~~ **claim 16**, wherein the RNA molecule is detected directly or indirectly by means of a labelled binding partner.

23. **(AMENDED)** A method according to claim 21 ~~[or 22]~~, wherein the labelled binding partner comprises DNA, RNA, LNA, PNA, or any combination thereof.

24. **(AMENDED)** A kit for use in performing ~~[the method of]~~**a method of detecting a nucleic acid sequence of interest,** any one of claims 16-23, comprising a probe molecule in accordance with ~~[any one of claims 1-14]~~ **claim 1**, and packaging means.

25. **(AMENDED)** A kit according to claim 24, further comprising one or more of the following: instructions for performing the method ~~[of any one of claims 16-23]~~; a buffer; a DNA polymerase; an RNA polymerase; deoxyribonucleotide triphosphates; ribonucleotide triphosphates; and a labelled binding partner.

26. A method of detecting a nucleic acid sequence of interest in a sample, the method comprising the steps of: contacting a nucleic acid probe molecule in accordance with ~~[any one of claims 1-14]~~ **claim 1** with a further probe and with a nucleic acid target molecule, which target is the sequence of interest or is formed as a result of the presence in the sample of the sequence of interest; causing the further probe molecule and the target molecule to hybridise adjacent each other to the probe molecule, thereby creating a functional double stranded RNA polymerase promoter; causing RNA synthesis from the RNA polymerase promoter, to create ~~[an]~~ **a** RNA molecule; and detecting directly or indirectly the RNA molecule so produced.